

Application No. 09/465,133  
Amendment Dated 6/16/2005

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### AMENDMENTS TO THE SPECIFICATION

Please amend the paragraph that begins on line 14 of page 32 as follows:

Chicken and mammalian progesterone are readily available and both function by binding to the same DNA regulatory sequence. Chicken progesterone receptor, however, binds a different spectrum of ligands, possessing different affinities from those interacting with human progesterone receptor. Thus, the chicken progesterone can be used as a transgene regulator in humans. Further, it can be used to screen for specific ligands which activate chicken progesterone receptor but not endogenous human progesterone receptor. An example of a ligand is 5-alpha-pregnane-3, 20-dione (dihydroprogesterone) which binds extremely well to chicken progesterone receptor but does not bind or binds very poorly to human progesterone receptor.

Please amend the paragraph that begins on line 24 of page 32 as follows:

Although the unmodified chicken progesterone receptor is already endowed with a different spectrum of ligand affinity from the human or other mammals and can be used in its native form, it is important to try to select additional mutated progesterone receptors to create a more efficacious receptor. The difference in chicken and human progesterone receptors are due to a few amino acid differences. Thus, other mutations could be artificially introduced. These mutations would enhance the receptor differences. Screening receptor mutations for ligand efficacy produces a variety of receptors in which alterations of affinity occur. The initial screening of progesterone mutants was carried out using intermediate levels of ligands. One mutant had lost progesterone affinity entirely, but bound a synthetic ligand RU38486 with nearly wild-type efficiency. RU38486 is normally considered an antagonist of progesterone function, but had become an agonist when tested using this specific mutant. Because the ligand is synthetic, it does not represent a compound likely to be found in the humans or animals to be treated with gene therapy. Although RU38486 works as an agonist in this case, it is not ideal because of its potential side effects as an anti-glucocorticoid. Further, it also binds to the wild-type human progesterone receptor. Thus it has the undesirable side effect of reproductive and endocrine disfunction.